

REMARKS

The Official Action of March 9, 2005 has been carefully considered and reconsideration of the application as amended is respectfully requested.

The claims have been amended to limit the recited R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, and R<sup>5</sup> groups so as to make the claims commensurate in scope with the evidence of record, as discussed below.

Claim 28 has been canceled so as to remove the basis for the claim objection appearing in the paragraph bridging pages 4-5 of the Official Action.

The claims stand rejected under 35 USC 103(a) as allegedly being unpatentable over Woods et al or over Woods et al in view of WO 92/16486 or WO 99/35150. Applicant respectfully traverses these rejections.

With the Amendment of August 25, 2004, Applicant submitted a Declaration under 37 CFR 1.132 signed by the inventor which presented evidence to show that the claimed compound provides unexpectedly enhanced antitumor activity as compared with the closest prior art compound. The Examiner has contended that the evidence in the declaration is not sufficient to rebut the alleged *prima facie* case of obviousness set forth by the cited art because: (a) the evidence was allegedly not commensurate in scope with the claims, and (b) the evidence allegedly only shows that the claimed invention works as intended. Applicant respectfully disagrees for reasons next discussed.

First, Applicant respectfully submits that, in view of the amendments to the claims, the evidence of unexpectedly advantageous results in the declaration is commensurate in scope with the claims. As discussed in MPEP Section 716.02(d), the nonobviousness of a broader claim

limitation can be supported by evidence based on unexpected results from testing a species if one of ordinary skill in the art would be able to determine a trend in the exemplified data which would allow the artisan to reasonably extend the probative value thereof. In the present case, it is clear from the specification as filed, including the Examples, that the exemplified dihydrogen phosphate compound is a prodrug which is hydrolyzed to the claimed hydroxy compound *in vivo* and that other salts, solvates, hydrates and prodrugs would be expected to behave similarly. In other words, the evidence in the specification, including the Examples, would allow one of skill in the art reasonably to extend the probative value of the evidence in the declaration to other salts, solvates, hydrates and prodrugs of the claimed species. Under these circumstances, it is respectfully submitted that the evidence in the declaration is commensurate in scope with the claims, which cover (only) the hydroxy compound and pharmaceutically acceptable salts, solvates, hydrates and prodrugs thereof.

With respect to the Examiner's contention that the Declaration shows only that the claimed compound works as intended, Applicant respectfully disagrees. Applicant respectfully notes in this regard that the Declaration shows that the claimed compound has antitumor activity against a tumor, round-cell sarcoma (SaS), that is resistant to combretastatin A4 phosphate (see Declaration at paragraphs 4 and 5). In contrast, combretastatin A4 was the most potent of the cis-stilbene compounds tested in the Woods et al article in inhibiting the growth of each of the tested cell lines (see Woods et al at page 708, column 2, second full paragraph, and Table IV).

Under these circumstances, one of skill in the art would have expected that, if combretastatin A-4 were not effective in inhibiting the growth of a tumor, the claimed

compound would not be effective either. The fact that the claimed compound is effective in inhibiting the growth of a tumor against which combretastatin A-4 is not effective is unexpected and probative of non-obviousness. See MPEP Section 716.02(a): "Evidence that a compound is unexpectedly superior in one of a spectrum of common properties . . . can be enough to rebut a *prima facie* case of obviousness." See, also, *In re Chupp*, 816 F.2d 643, 646, 2 USPQ2d 1437, 1439 (Fed. Cir. 1987) (Evidence showing that the claimed herbicidal compound was more effective than the closest prior art compound in controlling quackgrass and yellow nutsedge weeds in corn and soybean crops was sufficient to overcome the rejection under 35 U.S.C. 103, even though the specification indicated the claimed compound was an average performer on crops other than corn and soybean.).

For the above reasons, it is respectfully submitted that the Declaration of record provides evidence of unexpectedly advantageous results with the claimed compound that is sufficient to rebut any alleged *prima facie* case of obviousness set forth by the cited art. Accordingly, it is respectfully submitted that the prior art rejections of record have been overcome and that the application is now in allowable form. An early notice of allowance is earnestly solicited and is believed to be fully warranted.

Respectfully submitted,

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